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A NEW CHROMONE FROM *Angelica dahurica*

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In this study, a new chromone, six coumarins, and a phenolic compound were isolated from a MeOH extract of an Angelica dahurica *stems. Through the use of various spectral techniques, the structures of the isolated compounds were determined to be scopoletin (**1**), xanthyletin (**2**), xanthotoxin (**3**), hopeyhopin (**4**), thamnosmonin (**5**), 6-[(1*S*, 2*R*)-2,3-dihydroxy-1-methoxy-3-methylbutyl]-7-methoxycoumarin (**6**), decursidate (**7**), and new compound **8**, named dahuricalol. Among the isolatled and identified compounds, (*S*)-5-hydroxy-8-(hydroxymethyl)-2,2-dimethyl-6-oxo-3,4-dihydro-2*H*,6*H*-pyrano[3,2-g]chromen-3-yl (Z)-2-(hydroxymethyl)but-2-enoate (**8**) was isolated from plant for the first time.*

Keywords: *Angelica dahurica*, Apiaceae, stems, dihydropyronochromone, dahuricalol.

Angelica dahurica (Hoffm.) Benth. & Hook.f. ex Franch. & Sav. roots are commonly used in traditional Chinese medicine to treat common cold and headaches [1]. A number of chemical and biological studies have been conducted on the roots of this plant [2–11]. As part of an ongoing systematic phytochemical study about bioactive compounds in plants of the Apiaceae family from Korea, a detailed phytochemical study on the stem of *A. dahurica* was conducted to complement the phytochemical report on the same parts of this plant [12]. In this study, the isolation and structure elucidation of a new compound from the stem of *A. dahurica* are described.

The UV spectrum of compound **8** showed λ_{max} values at 209, 228, 251, 257, and 296 nm, which suggested that this compound had a chromone skeleton [13]. The molecular formula of compound **8** was determined to be $C_{20}H_{22}O_8$ by HR-EI-MS, the spectrum of which showed a molecular ion peak at *m/z* 390.1316 (calcd for 390.1315). The ^{1}H NMR spectrum of compound **8** exhibted two singlets at δ_H 6.39 and 6.29, a hydroxymethyl signal at δ_H 4.46, a triplet at δ_H 5.24 (J = 4.8 Hz), two sets of double doublets at δ_H 3.01 (J = 17.6, 4.9 Hz) and 2.83 (J = 17.6, 4.6 Hz), and two methyl singlets at δ_H 1.40 and 1.38, which correlated with the carbon signals at δ_C 95.9, 106.5, 61.4, 71.1, 23.5, 25.0, and 23.7 in its HSQC spectrum. Furthermore, its ^{13}C NMR spectrum showed a γ-pyrone carbonyl signal at δ_C184.2, an olefinic quaternary carbon at δ_C 171.9, five aromatic quaternary carbon signals at δ_C 160.7, 160.6, 157.5, 106.5, 105.6, and 103.9, and an oxygen-bearing aliphatic quaternary carbon signal at δ_C 78.4. Based on its NMR signals, which included a triplet at δ_H 5.24, two sets of double doublets at δ_H 3.01 and 2.83, two methyl singlets at δ_H 1.40 and 1.38, and carbon signals at δ_C 78.4, 71.1, 25.0, 23.7, and 23.5, compound **8** has a dimethyldihydropyran ring in its chromone skeleton [14]. In the HMBC spectrum of compound **8**, the hydroxymethyl signal at δ_H 4.46 correlated with the signal at δ_C 171.9, indicating a hydroxymethyl moiety at its C-2 position. In addition, the NMR spectra of compound **8** indicated the presence of an acyl moiety at δ_H 6.35 (1H, q, J = 7.3 Hz), 4.14 (2H, m), and 1.90 (3H, d, J = 7.3 Hz) and δ_C 167.3, 140.3, 133.4, 64.7, and 15.6. These NMR signals were very similar to those of the angeloyl moiety, except for the presence of a hydroxymethyl group signal (δ_H 4.14; δ_C 64.7) instead of a methyl signal in the acyl moiety [15], which was confirmed by mass fragmentations at *m/z* 98 ($C_5H_6O_2$) and 292 ($M - C_5H_6O_2$). In the HMBC spectrum of compound **8**, the acyl hydroxymethyl signal at δ_H 4.14 was correlated with the signals at δ_C 167.3, 140.3, and 133.4, indicating that the hydroxymethyl signal was attached at the α-position of its angeloyl group. This finding was confirmed using a NOESY spectrum analysis, which verified the correlation between the signals at δ_H 4.14 and 6.35 (Fig. 1).

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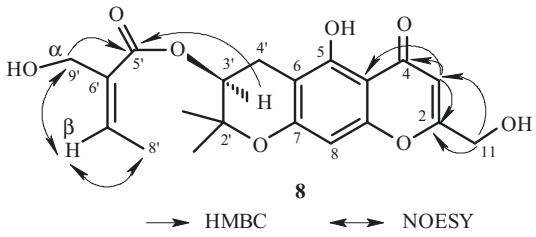

Fig. 1. Important HMBC and NOESY correlations of compound **8**.

The HMBC spectrum of the compound showed a correlation between the H-3′ signal at δ_H 5.24 and the acyl carbonyl signal at δ_C 167.3, which suggested that the acyl moiety of compound **8** was located at the C-3′ position of the dihydropyranochromone skeleton. The absolute configuration of the C-3′ position of compound **8** was determined as *S* from the negative value (–10.4) at 227 nm and the positive value (+9.6) at 255 nm in its CD spectrum [13]. These spectral data allowed us to establish the structure of compound **8** as (*S*)-5-hydroxy-8-(hydroxymethyl)-2,2-dimethyl-6-oxo-3,4-dihydro-2*H*,6*H*-pyrano[3,2-g]chromen-3-yl (*Z*)-2-(hydroxymethyl)but-2-enoate, which could not be found in structural databases, such as SciFinder and Google Scholar. Thus, we named compound **8** of dahuricalol.

Compounds **1**–**7** were identified as scopoletin [12], xanthyletin [16], xanthotoxin [17], hopeyhopin [18], thamnosmonin [19], 6-[(1*S*,2*R*)-2,3-dihydroxy-1-methoxy-3-methylbutyl]-7-methoxycoumarin [12], decursidate [16], respectively, by comparing their spectral data with those reported in the literature.

EXPERIMENTAL

General. UV spectra were obtained using a Jasco V-530 UV/Vis spectrophotometer (Jasco, Tokyo, Japan). Optical rotations were recorded using a Jasco DIP-100 digital polarimeter (Jasco, Tokyo, Japan). NMR spectra were obtained using a Bruker Avance Neo 600 instrument (Bruker, Rheinstetten, Germany). HR-EI-MS spectra were obtained using a JMS-700 mass spectrometer (Jeol, Tokyo, Japan). Silica gel (Merck Kieselgel 60, 63–200, and 40–63 μm), reversed-phase silica gel (YMC gel ODS-A, 150 μm), and Sphadex LH-20 (Amersham Pharmacia Biotech) were used for the column chromatography (CC). Extra pure solvents (DaeJung Co., Shiheung, Korea) were used for CC. TLC was performed on a glass backed Kieselgel 60 F_{254} and RP F_{254s} plates and visualized by 20% (v/v) H_2SO_4.

Plant Material. The stems of *A. dahurica* were collected from Jungseon, Gangwondo Province in August 2016. A voucher specimen (KNUH-S-1608-3) was deposited in the Herbarium of the College of Pharmacy, Kangwon National University, Korea.

Extraction and Isolation. The *A. dahurica* stems (2.6 kg) were air-dried, cut into small pieces, and extracted three times with MeOH (14 L) at 80°C under reflux for 4 h. All extracts were filtered and concentrated *in vacuo* at 40°C. The MeOH extract (311 g) was suspended in water and successively partitioned with *n*-hexane, $CHCl_3$, and *n*-BuOH, leaving a residual water-soluble fraction. The *n*-hexane, $CHCl_3$, and *n*-BuOH soluble fractions were evaporated *in vacuo* to yield the residues of the *n*-hexane (20 g), $CHCl_3$ (60 g), and *n*-BuOH (22 g) fractions. The $CHCl_3$ fraction (58 g) was subjected to silica gel CC with stepwise gradient elution using an $CHCl_3$–MeOH system (19:1–1:1) to obtain five fractions (ADC-1–5). Fraction ADC-1 (1.1 g) was re-chromatographed on silica gel and ODS CC to obtain compounds **1** (105.7 mg), **2** (6.6 mg), and **3** (3.6 mg). Fraction ADC-2 (8.4 g) was fractionated using silica gel CC to obtain compound **4** (87.4 mg). The ADC-3 fraction (32 g) was re-chromatographed over ODS CC isocratic elution using MeOH–H_2O (60:40) to obtain five fractions (ADC-3-1–3-5). Fraction ADC-3-1 (0.5 g) was subjected to silica gel CC with isocratic elution using *n*-hexane–EtOAc (1:1) to obtain compounds **5** (20.7 mg) and **6** (74.9 mg). Fraction ADC-4 (3.1 g) was further fractionated using silica gel with benzene–EtOAc (2:1) to obtain four fractions (ADC-4-1–4-4). Fraction ADC-4-2 (1.2 g) was re-chromatographed over ODS CC isocratic elution with MeOH–H_2O (55:45) to obtain compound **7** (55.4 mg). Fraction ADC-4-4 (0.2 g) was purified by passing it through Sephadex LH-20 (MeOH–H_2O, 50:50) to obtain compound **8** (33 mg).

Dahuricalol (8), white powder, $[\alpha]_D^{20}$ –21° (*c* 0.15, MeOH). UV (MeOH, λ_{max}, nm): 209, 228, 251, 227, 296. CD (*c* 0.1, MeOH, λ_{max}, nm) (Δε): 227 (–10.4), 255 (+9.6). ^{1}H NMR (600 MHz, MeOH-d_4, δ, ppm, J/Hz): 6.39 (1H, s, H-8), 6.35 (1H, q, J = 7.3, *β*-H), 6.29 (1H, s, H-3), 5.24 (1H, t, J = 4.8, H-3′), 4.46 (2H, s, H-11), 4.14 (2H, m, H-9′), 3.01 (1H, dd,

J = 17.6, 4.9, Hb-4′), 2.83 (1H, dd, J = 17.6, 4.6, Ha-4′), 1.90 (3H, d, J = 7.3, H-8′), 1.40 (3H, s, CH_3-2′), 1.38 (3H, s, CH_3-2′). ^{13}C NMR (150 MHz, MeOH-d_4, δ, ppm): 184.2 (C-4), 171.9 (C-2), 167.3 (5′-C=O), 160.7 (C-7), 160.6 (C-5), 157.5 (C-9), 140.3 (C-7′), 133.4 (C-6′), 106.5 (C-3), 105.6 (C-10), 103.9 (C-6), 95.9 (C-8), 78.4 (C-2′), 71.1 (C-3′), 64.1 (C-9′), 61.4 (C-11), 25.0 (CH_3-2′), 23.7 (CH_3-2′), 23.5 (C-4′), 15.6 (C-8′). HR-EI-MS *m/z* 390.1316 (calcd for $C_{20}H_{22}O_8$, 390.1315); EI-MS *m/z* ($I_{rel.}$, %): 390 $[M]^+$ (2.2), 292 (4.5), 274 (46.4), 259 (100), 257 (75), 252 (14), 250 (8.8), 243 (9.5), 221 (16.9), 203 (5.1), 129 (3.6), 115 (3.5), 98 (5.3), 83 (3.0).

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